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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/896,589	07/17/1997	MARTIN KARL RUSSEL BURNHAM	P50533-03	3376

7590 10/03/2003

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	12

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/896,589	BURNHAM ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 1999* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-26,68-73 and 83-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,68-73 and 83-101* is/are rejected.

7)☒ Claim(s) *24 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant is advised that the Notice of Allowance mailed is vacated. If the issue fee has already been paid, applicant may request a refund or request that the fee be credited to a deposit account. However, applicant may wait until the application is either found allowable or held abandoned. If allowed, upon receipt of a new Notice of Allowance, applicant may request that the previously submitted issue fee be applied. If abandoned, applicant may request refund or credit to a specified Deposit Account.

2. Prosecution on the merits of this application is reopened on claims 24-26, 68-73 & 83-101 considered unpatentable for the reasons indicated below:

Claims found previously allowable have 112 first and second paragraphs issues which need to be addressed and is indicated in the rejections outlined in this Office Action.

3. Claims 24-26, 68-73 & 83-101 are pending and under consideration in this examination.

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. ***Claim Rejections - 35 U.S.C. § 112*** (first paragraph)

Deposit Requirement

Claim 68, 92-94 & 101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention. It is apparent that the [plasmid/microorganism/vector] is required to practice the claimed invention. As such the [plasmid/microorganism/vector] must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the [plasmid/microorganism/vector]. The specification lacks complete deposit information for the deposit of [plasmid/microorganism/vector]. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, (c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the

biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

Claims 68, 92-94 & 101 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

While deposits of NCIMB Numbers 40794 have been made in accordance Budapest Treaty at a recognized depository; however, an affidavit or declaration [under 37 CFR 1.808] stating that : all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, and the deposit will be replaced if it should ever become inviable, is not provided.

6. ***Enablement***

Claims 83-101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide of SEQ ID NO: 1 encoding a xanthine phosphoribosyl transferase of SEQ ID NO : 2, does not reasonably provide enablement for any polynucleotide sequence of Formula X-$(R_1)_n$-1-[PN-SEGMENT]-AA-$(R_2)_n$-Y or a variant, fragment or derivative thereof, or vectors or host cells comprising such modified polynucleotides (claims 70-73 & 83-101) or isolated polynucleotides share 90% (10 substitution, deletion or insertions per 100 nucleotides), 95% (5 substitution, deletion or insertions per 100 nucleotides) or 95% sequence homology to SEQ ID NO : 1. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 83-101 encompass any polynucleotide (or vector, host cell or method of making the transferase), which by definition of the Formula in claim 84 or modification by substitution, deletion or insertion comprise a variant, fragment or derivative thereof. The scope of the claims do not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotide fragments or variants broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of xanthine phosphoribosyl transferase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

The specification does not support the broad scope of the claims which encompass all modifications (5-10%) and/or fragments/segments of polynucleotide of SEQ ID NO : 1 or the formula whereby the polynucleotide is modified further, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting xanthine phosphoribosyl transferase activity; (B) the general tolerance of xanthine phosphoribosyl transferase to modification (mutational or terminal) and extent of such tolerance; (C) a rational and predictable scheme for modifying any xanthine phosphoribosyl transferase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Further, the no assay system for xanthine phosphoribosyl transferase is provided in order that a skilled artisan is able to measure the enzyme activity in the randomized modified xanthine phosphoribosyl transferase. Therefore, random modifications of the SEQ ID NO : 1 or the fragments or derivatives of Formula, without adequate guidance, may result in a polynucleotide encoding a protein with no xanthine phosphoribosyl transferase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any xanthine phosphoribosyl transferase encoding polynucleotide with a number of modifications of SEQ ID NO : 1 and be able

to express a viable and functional protein. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of variously modified polynucleotides encoding polypeptides having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

7.. ***35 U.S.C. § 112, first paragraph (Written Description)***

Claims 83-101 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 83-101 encompass any polynucleotide (or vector, host cell or method of making the transferase), which by definition of the Formula in claim 84 or modification by substitution, deletion or insertion comprise a variant, fragment or derivative thereof.

The specification, however, only provides a single representative species of the genus comprising SEQ ID NO :1 (and the encoding SEQ ID NO : 2, having the transferase activity). There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species or modify the sequence(s) of formula or SEQ ID NO : 1 or segments thereof, by substitution, deletion or addition in order to make a polynucleotide capable of expressing a

polypeptide having xanthine phosphoribosyl transferase activity. The specification also fails to describe additional representative species of such polynucleotides by a identifying structural characteristics relevant to such modifications other than sequence of SEQ ID Nos. 1 & 2, or the vague formula recited in claim 84, for which no predictability of structure/activity is apparent. Given this lack of additional representative species, such as the modifications in order to crate a variant, fragment or derivative of the Formula and still have some activity and/or utility, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Therefore, the written description requirement is not satisfied.

8. Claim 68 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 68, depends upon a canceled claim 30. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

9. Claims 24 & 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. ***Claim Rejections - 35 U.S.C. § 112*** (second paragraph)

Claims 25 & 69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25, lines 2-3, recite 'comprises nucleotide from position 1-579 inclusive of the polynucleotide sequence of SEQ ID NO : 1'.

Claim 69, lines 1-2, recite 'comprising nucleotide from position 1-579 inclusive of the polynucleotide sequence set forth in SEQ ID NO : 1'.

The claims are indefinite because : (1) comprises or comprising nucleotides (plural) is required; and (2) positions 1-579 cannot be inclusive of SEQ ID NO : 1, because SEQ ID NO : 1 consists of 582 nucleotides.

11. Claims 70-73 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 70, recites '....polypeptide comprising a region having an amino acid sequence of SEQ ID NO : 2'. The claims are indefinite because it is not clear because SEQ ID NO : 2 is full length sequence and what region of the polypeptide refers to having a sequence of SEQ ID NO : 2.

Rephrasing the claim – to read : '.....polypeptide comprising an amino acid sequence of SEQ ID NO : 2', will overcome this rejection.

Claims 71-73 are included in the rejection for failing to correct the defect present in the base claim.

12. No claim is allowed.

13. Claims drawn to full length sequences will be in better condition for allowance.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

T K Saidha

Tekchand Saidha
Primary Examiner, Art Unit 1652
October 1, 2003